REMARKS

I. Status of the Claims

Claims 1-112 and 126-144 were previously canceled. Claims 113-125 are pending. Applicants note with appreciation that the Examiner has indicated the allowability of claim 116 and claim 115, except for the dependency of the latter from a rejected claim.

II. Claim Rejections

A. 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 113, 114, and 117-125 under 35 U.S.C. §112, first paragraph, for alleged failure to meet the written description requirement. Specifically, the Examiner objected to the limitation of "at least 90% identity to SEQ ID NO:6" introduced by Applicants' previous amendment and alleged that it is not fully supported by the specification as originally filed. Applicants respectfully traverse the rejection.

Pointing to the paragraph beginning on page 9, line 18, of the specification, the Examiner argued that the description allows gaps in the sequence percentage calculation and further eluded to a 96.5% identity between SEQ ID NO:6 of the present application and SEQ ID NO:2 of U.S. Patent No. 5,869,445 ("the '445 patent"). Because SEQ ID NO:6 of the present application is the amino acid sequence of a direct fusion of human HER-2/neu ECD-PD, and SEQ ID NO:2 of the '445 patent is the full-length sequence of human HER-2/neu protein, the Examiner reasoned that the new limitation of the HER-2/neu fusion protein having "at least 90% identity to SEQ ID NO:6" is contradictory to the other limitation of the HER-2/neu fusion protein "consisting of a HER-2/neu extracellular domain fused to a HER-2/neu phosphorylation domain" and therefore concluded that the new limitation "changes the scope of 'HER-2/neu fusion protein' as originally disclosed. See the last paragraph on page 3 to the first full paragraph on page 4 of the Office Action mailed May 9, 2005.

The Examiner's position is untenable. First of all, Applicants note that the 96.5% sequence identity between SEQ ID NO:2 of the '445 patent and SEQ ID NO:6 of the present application is obtained in a manner inconsistent with the description of the instant specification.

As the Examiner has correctly pointed out, the specification describes how percentage sequence identity is calculated on page 9, lines 18-26, stating that,

> "Percentage of sequence identity" is determined by comparing two optimally aligned sequences over a comparison window, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. ***The percentage is calculated by determining the number of positions at which the identical nucleic acid base or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison and multiplying the result by 100 to yield the percentage of sequence identity*** (emphasis added).

It is therefore clear that gaps are allowed in achieving optimal sequence alignment and that the residues within the gaps are a part of the comparison window. This description also indicates that, in calculating percentage sequence identity between two amino acid sequences, such as SEQ ID NO:2 of the '445 patent and SEQ ID NO:6 of the instant application, the numerator is the number of identical residues within the window of comparison, whereas the denominator is "the total number of positions in the window of comparison."

SEQ ID NO:2 of the '445 patent is the full-length sequence of human HER-2/neu protein with 1255 amino acids, and SEQ ID NO:6 of the present application is the sequence of a direct fusion of human HER-2/neu ECD and PD with 919 amino acids. In other words, SEQ ID NO:6 of the present application is SEQ ID NO:2 of the '445 patent with a deletion spanning from residues 654 to 997 of SEQ ID NO:2. According to the method of calculation described in the paragraph quoted above, the sequence identity between SEQ ID NO:2 and SEQ ID NO:6 should therefore be 919 ÷ 1255 x 100% = 73.2%. This is exactly the same percent identity shown in the Examiner's sequence alignment results (indicated as "best local similarity"). Applicants are uncertain, and the Examiner has not explained, what calculation method was used to obtain the "query match" value of 96.5%, which is indicated above the "best local similarity" value in the Examiner's sequence alignment results. What Applicants are certain is, when using the sequence

percent identity calculation method explicitly described by the specification, SEQ ID NO:2 of the '445 patent has only 73.2% identity to SEQ ID NO:6 of the present application.

Secondly, even if the 96.5% sequence identity between SEQ ID NO:2 of the '445 patent and SEQ ID NO:6 of the present application were properly obtained by calculation according to the method taught by the instant specification, the new limitation of "at least 90% identity to SEQ ID NO:6" still would not necessarily contradict the pre-existing limitation of "consisting of a HER-2/neu extracellular domain fused to a HER-2/neu phosphorylation domain," since the sequence of SEQ ID NO:6 or with one or two substitutions would certainly possess both limitations. The new limitation and the pre-existing limitation are therefore not mutually exclusive.

Moreover, by alleging the new limitation of "at least 90% identity to SEQ ID NO:6" contradictory to the pre-existing limitation of "consisting of a HER-2/neu extracellular domain fused to a HER-2/neu phosphorylation domain," the Examiner appeared to argue that a claim amendment cannot properly introduce a new limitation that, when considered alone, would define a genus that would not completely overlap the genus defined by pre-existing claim limitations. Yet, there is no such requirement under 35 U.S.C. §112, second paragraph. As set forth in MPEP §2163, the written description requirement is met if the claimed subject matter defined by a new claim limitation is adequately described in the original disclosure. This is precisely the case here.

As such, Applicants submit that the written description rejection under 35 U.S.C. §112, second paragraph, is improper. Its withdrawal is hereby respectfully requested.

B. 35 U.S.C. §102 and 103

The Examiner further rejected the pending claims under 35 U.S.C. §102 for alleged anticipation by the '445 patent and under §103 for alleged obviousness over the '445 patent in view of secondary references WO91/18926, WO95/17210, and WO96/20555. Applicants understand that these rejections were made on the premises that SEQ ID NO:2 of the '445 patent is an amino acid sequence that has "at least 90% identity to SEQ ID NO:6."

As discussed above, when sequence alignment results are properly interpreted according to the specification, SEQ ID NO:2 of the '445 patent does not have "at least 90% identity to SEQ ID NO:6." As such, the limitation of "at least 90% identity to SEQ ID NO:6" is not found in the '445 patent. Nor is it present in any of the secondary references. The anticipation and obviousness rejections are thus improper.

The rejections under 35 U.S.C. §102 and §103 are further improper because the pending claims recite that the HER-2/Neu fusion protein "consist[s] of a HER-2/neu extracellular domain fused to a HER-2/neu phosphorylation domain." In contrast, SEQ ID NO:2 of the '445 patent does contain a HER-2/Neu transmembrane domain and portions of the intracellular domain beyond the phosphorylation domain. Therefore, this particular claim limitation is not found in the '445 patent. The secondary references also fail to provide this limitation.

The withdrawal of the anticipation and obviousness rejections is thus respectfully requested.

III. Priority

The Examiner contended that the present application is only entitled to the actual filing date of May 9, 2001, apparently taking the position that the claim amendment introducing the limitation of "at least 90% identity to SEQ ID NO:6" renders the claimed subject matter ineligible for the benefit of the priority documents, or the effective filing date of January 29, 1999. For reasons stated in above, the limitation of "at least 90% identity to SEQ ID NO:6" is indeed adequately supported by the specification as originally filed and by the priority applications. Thus, the claimed subject matter is entitled to the January 29, 1999, filing date.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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